

## General

### Guideline Title

Systematic screening for active tuberculosis: principles and recommendations.

### Bibliographic Source(s)

World Health Organization (WHO). Systematic screening for active tuberculosis: principles and recommendations. Geneva (Switzerland): World Health Organization (WHO); 2013. 133 p. [103 references]

### Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

## Recommendations

### Major Recommendations

The rating schemes for the quality of the evidence (high, moderate, low, very low) and the strength of the recommendations (strong, conditional) are defined at the end of the "Major Recommendations" field.

#### Key Principles for Screening for Active Tuberculosis (TB)

The following key principles should be considered when planning a TB screening initiative.

1. Before screening is initiated, high-quality TB diagnosis, treatment, care, management and support for patients should be in place, and there should be the capacity to scale these up further to match the anticipated rise in case detection that may occur as a result of screening. In addition, a baseline analysis should be completed in order to demonstrate that the potential benefits of screening clearly outweigh the risks of doing harm, and that the required investments in screening are reasonable in relation to the expected benefits.
2. Indiscriminate mass screening should be avoided. The prioritization of risk groups for screening should be based on assessments made for each risk group of the potential benefits and harms, the feasibility of the initiative, the acceptability of the approach, the number needed to screen, and the cost effectiveness of screening.
3. The choice of algorithm for screening and diagnosis should be based on an assessment of the accuracy of the algorithm for each risk group considered, as well as the availability, feasibility and cost of the tests.
4. TB screening should follow established ethical principles for screening for infectious diseases, observe human rights, and be designed to minimize the risk of discomfort, pain, stigma and discrimination.
5. The TB screening approach should be developed and implemented in a way that optimizes synergies with the delivery of other health services and social services.

6. A screening strategy should be monitored and reassessed continually to inform re-prioritization of risk groups, re-adaptation of screening approaches when necessary and discontinuation of screening at an appropriate time.

See section 7 in the original guideline document for details on the key principles.

#### Recommendations on Risk Groups to Be Screened for Active TB

##### Strong Recommendations

###### *Recommendation 1*

Household contacts and other close contacts should be systematically screened for active TB. (Strong recommendation, very low-quality evidence)

###### *Recommendation 2*

People living with human immunodeficiency virus (HIV) should be systematically screened for active TB at each visit to a health facility. (Strong recommendation, very low-quality evidence)

###### *Recommendation 3*

Current and former workers in workplaces with silica exposure should be systematically screened for active TB. (Strong recommendation, low-quality evidence)

##### Conditional Recommendations

###### *Recommendation 4*

Systematic screening for active TB should be considered in prisons and other penitentiary institutions. (Conditional recommendation, very low-quality evidence)

###### *Recommendation 5*

Systematic screening for active TB should be considered in people with an untreated fibrotic lesion seen on chest X-ray. (Conditional recommendation, very low-quality evidence)

###### *Recommendation 6*

In settings where the TB prevalence in the general population is 100/100 000 population or higher, systematic screening for active TB should be considered among people who are seeking health care or who are in health care and who belong to selected risk groups (see Table 9 in the original guideline document for information on risk factors). (Conditional recommendation, very low-quality evidence)

###### *Recommendation 7*

- a. Systematic screening for active TB may be considered for geographically defined subpopulations with extremely high levels of undetected TB (1% prevalence or higher).
- b. Systematic screening for active TB may be considered also for other subpopulations that have very poor access to health care, such as people living in urban slums, homeless people, people living in remote areas with poor access to health care, and other vulnerable or marginalized groups including some indigenous populations, migrants and refugees. (Conditional recommendation, very low-quality evidence)

See section 8 in the original guideline document for remarks on these recommendations.

#### Definitions:

#### Grading of Recommendations Assessment, Development and Evaluation (GRADE) Levels of Evidence

Quality of Evidence	Rationale
High	Further research is very unlikely to change confidence in the estimate of effect.
Moderate	Further research is likely to have an important impact on confidence in the effect.

<b>Quality of Evidence</b>	<b>Rationale</b>
<b>Very Low</b>	Any estimate of effect is very uncertain.

## Strength of Recommendations

A strong recommendation is one for which the desirable effects of adhering to the recommendation are judged to clearly outweigh the undesirable effects; for these recommendations screening is judged to be feasible, acceptable and affordable in all settings. The Guideline Development Group placed a high value on ensuring that TB is diagnosed early in groups with a particularly high likelihood of having undetected TB and at a high risk for poor health outcomes in the absence of early diagnosis and treatment even if direct evidence of the benefits of screening were lacking. This is the rationale for making strong recommendations despite a lack of high-quality direct evidence for some risk groups.

A conditional recommendation is one for which the desirable effects of adhering to the recommendation probably outweigh the undesirable effects but the trade-offs, cost effectiveness, feasibility or affordability, or a combination of these, are uncertain. Reasons for uncertainty may include:

- A lack of high-quality evidence to support the recommendation
- Evidence of limited benefits from implementing the recommendation
- High costs, or low feasibility or acceptability, or a combination of these.

The degree of uncertainty about the trade-offs between the desirable effects and undesirable effects of adhering to each of the conditional recommendations varies across settings, and depends on the epidemiological situation and the health system. Therefore, a conditional recommendation in this guideline implies that:

- The appropriateness of adhering to the recommendation needs to be assessed in each setting.
- There is a need to prioritize screening across risk groups in each setting.

## Clinical Algorithm(s)

Algorithms for screening and diagnosis of tuberculosis are provided in Annex III in the original guideline document. Discussion of the algorithms is provided in Section 9 in the original guideline document.

# Scope

## Disease/Condition(s)

Active tuberculosis (TB)

## Guideline Category

Diagnosis

Risk Assessment

Screening

## Clinical Specialty

Family Practice

Infectious Diseases

Internal Medicine

Pediatrics

Pulmonary Medicine

## Intended Users

Advanced Practice Nurses

Health Care Providers

Nurses

Physician Assistants

Physicians

Public Health Departments

## Guideline Objective(s)

To provide evidence-based:

- Key principles to guide the planning and implementation of systematic screening for active tuberculosis (TB)
- Recommendations on prioritizing risk groups for systematic screening for active TB
- Algorithm options for screening and diagnosis of active TB

## Target Population

People with suspected active tuberculosis (TB), in a predetermined target group

## Interventions and Practices Considered

Systematic screening for active tuberculosis (TB): risk groups to be screened

## Major Outcomes Considered

- Tuberculosis (TB) case detection
- Outcomes from TB treatment
- Prevalence and incidence of TB
- Sensitivity and specificity/accuracy of different diagnostic tests
- Number needed to screen
- Acceptability of screening

## Methodology

### Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

## Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse and the World Health Organization (WHO): In order to develop the principles and recommendations for systematic screening for active tuberculosis, WHO commissioned four systematic reviews (see the "Availability of Companion Documents" field).

### Review 1: The Benefits to Communities and Individuals of Screening for Active Tuberculosis Disease: a Systematic Review

#### Specific Questions

The review addressed four specific questions:

1. Does screening for tuberculosis (TB) disease increase the number of TB cases detected compared to passive case finding (PCF)?
2. Does screening for TB disease identify cases at an earlier stage of TB disease than PCF?
3. Is there a difference in treatment outcomes between TB cases found by screening and those found through PCF?
4. Does the addition of screening for TB disease to PCF affect TB incidence or prevalence in the community?

#### Search Strategy

The initial search used papers selected on initial screening by an existing systematic review which had already identified TB case-finding studies published up to 13 October 2010. This review searched online databases PubMed, EMBASE and SCOPUS from 1980 to 2010 to identify titles and abstracts of peer-reviewed papers that met the criteria for initial review. The detailed search strategy is outlined in Appendix Table A.1.

Titles and abstracts identified by the search terms were entered into a database, duplicates were eliminated and the remaining entries were independently screened by two readers for inclusion in the next stage of review. Discrepancies were resolved by consensus and/or consultation with a third reader.

In addition to online databases, abstracts from 2008 to 2010 of the conferences of the International AIDS Society (AIDS/IAS), the International Union Against Tuberculosis and Lung Disease and the American Thoracic Society were searched to identify the most recent research conducted on screening strategies. No exclusions were made on the basis of study population, geographical setting or year of publication.

#### Selection of Publications for Inclusion

The full texts of all publications identified by the existing systematic review were screened for relevance for any of the four outcomes. This was done in stages: an initial screen to check for possible eligibility, then a more detailed screening of retained papers, followed by data extraction of eligible publications. The first 120 publications reviewed in the initial screening were done in duplicate to ensure consistency, and all data extraction of included papers was done in duplicate using a standardised data extraction tool. Any discrepancies were resolved by discussion.

See the review for details on search strategy and inclusion criteria.

### Review 2: A Systematic Review of the Sensitivity and Specificity of Symptom and Chest-radiography Screening for Active Pulmonary Tuberculosis in HIV-negative Persons and Persons with Unknown HIV Status

#### Search Strategy

Reviewers searched online data bases MEDLINE, EMBASE, LILACS and HTA (Health Technology Assessment) from 1992 to 2012, up till 2nd July 2012, to identify titles and abstracts of peer-reviewed papers that met criteria for initial review. Search terms included combinations of three domains: (1) "tuberculosis" and related terms; (2) terms related to "screening", "survey", "sensitivity", "specificity"; and (3) search terms related to the reference standard, "bacterial culture", "microscopy". A complete list of search terms for each database is provided in Appendix 1.

In addition, reference lists of relevant reviews and studies were checked, the websites of the WHO Stop TB department were searched and experts were asked for relevant studies and unpublished reports. Unpublished reports were only included if permission was granted by the investigators.

The titles and abstracts of the records that remained after electronic removal of duplicates were independently reviewed by two reviewers, to identify records that were possibly eligible for inclusion in the next review stage.

See review for additional information on search strategy and details on inclusion criteria.

### Review 3: A Systematic Review of the Number Needed to Screen to Detect a Case of Active Tuberculosis in Different Risk Groups

#### Selection of Papers and Abstracts to Include

Reviewers searched online databases PubMed, EMBASE, and SCOPUS from 1980 to 2010 to identify titles and abstracts of peer-reviewed papers that met criteria for initial review. Due to the lack of standardization of terminology historically used to describe active case-finding, search terms were broad and intended to maximize sensitivity of the search to relevant papers. Search terms included combinations of "tuberculosis," "TB," "consumption," "phthisis," with "active case-finding," "intensified case-finding," "mass chest X-ray," "chest radiography," "contact screening," "contact examination," "prevalence survey," and "screening" among other terms. A complete list of search terms for each database can be found in Appendix A.

Titles and abstracts identified by the search terms were entered into a database, duplicates were eliminated, and remaining entries were independently screened by two readers for inclusion in the next stage of review. Discrepancies were resolved by consensus and/or consultation with a third reader.

In addition to online databases, abstracts from 2008 to 2010 of the conferences of the International AIDS Society (AIDS/IAS), the International Union Against Tuberculosis and Lung Diseases, and the American Thoracic Society were searched to identify the most recent research conducted on active case-finding strategies.

See the review for information on review process and inclusion criteria.

### Review 4a: Acceptability of TB Screening among At-risk and Vulnerable Groups: a Systematic Qualitative/Quantitative Literature Metasynthesis

#### Data Collection Process

##### *Quantitative Search Strategy*

1. A total of 32 literature searches were conducted in two databases - Institute for Scientific Information (ISI) WEB of Science and EMBASE (see Appendix 2 of the original systematic review)
2. Reviewers collaborated with the TB Screening Group at Johns Hopkins University (JHU) to identify relevant studies.
3. The reference lists, appendices, and supplementary web material of the index article were hand-searched to identify key resources.
4. Reviewers consulted colleagues to identify manuscripts in preparation on studies in hidden populations and on risk groups for which little was published in peer review journals (e.g., men who have sex with men [MSM], sex workers, adolescents).

See the review for additional information.

### Review 4b: Acceptability of Household and Community-based TB Screening in High Burden Communities: a Systematic Literature Review

Four online databases (Web of Science, PubMed [Medline], LILACS, and EMBASE) were searched for the publication years 2000-2011 to identify studies. In addition, reviewers searched abstracts of the International Union Against Tuberculosis and Lung Disease (IUATLD/UNION) and the International Tuberculosis Surveillance Research Unit (TSRU) conferences by manually screening the abstract books and CD ROMs for the period 2000-2011. Additional papers were identified through searching references and via scrutiny of a power point presentation on a systematic review of active case-finding strategies for TB, which was carried out by Johns Hopkins University and the systematic literature review by Kranzer et al. (2011). Unpublished reports were only included if permission was granted by the investigators.

See the review for information on study selection process and inclusion/exclusion criteria.

## Number of Source Documents

### Review 1: The Benefits to Communities and Individuals of Screening for Active Tuberculosis Disease: a Systematic Review

A total of 31,915 publications and 79 abstracts were identified in the previous search. In addition, unpublished studies and studies identified through expert opinion, prevalence surveys from Cambodia and Myanmar and conference abstracts and unpublished reports from the ZAMSTAR study were reviewed, and 21 relevant studies identified; 1811 publications were identified for full-text review after removal of duplicates and screening of the titles and abstracts. Of these, 963 were excluded on an initial screen and 786 subsequently, leaving 62 publications that addressed at least one of the study questions. See the Appendix figure in the review (see the "Availability of Companion Documents" field) for more information.

### Review 2: A Systematic Review of the Sensitivity and Specificity of Symptom and Chest-radiography Screening for Active Pulmonary

## Tuberculosis in HIV-negative Persons and Persons with Unknown HIV Status

From the online database search 3596 titles and abstracts were identified after (electronic) removal of duplicates.

Fifty-eight studies with a focus on young children (0-5 years old) or pediatric tuberculosis (TB) only were taken to a separate database. Of those, only one study evaluated a screening tool in human immunodeficiency virus (HIV)-negative children and is described in Appendix 2 in the review.

Of the 225 titles and abstracts that were identified to obtain full text to further assess eligibility, 4 appeared duplicates, 8 were conference abstracts, 11 were ineligible due to language (Chinese or Russian). Of 14 the full text could not be retrieved, in none of the latter the title or abstract directly suggested an evaluation of a symptom or chest radiography (CXR) screening tool.

Out of the online database search 21 publications were identified for inclusion. In addition three publications were identified through the World Health Organization (WHO) website and the authors. Those 24 publications reported on 17 studies.

### Review 3: A Systematic Review of the Number Needed to Screen to Detect a Case of Active Tuberculosis in Different Risk Groups

A total of 28,206 titles and abstracts were identified from electronic databases. After removal of duplicates and studies not meeting inclusion criteria, a total of 1737 publications were identified for full-text review. Of these, 601 papers and abstracts were included. Nine additional conference abstract sets were reviewed for keywords. A total of 606 individual studies were included in the final analysis which are summarised in Table 1 in the review.

### Review 4a: Acceptability of TB Screening among At-risk and Vulnerable Groups: a Systematic Qualitative/Quantitative Literature Metasynthesis

The numbers of studies screened, assessed for eligibility, and included in the review, are outlined in tabular form (see Table 4 in the review). Reasons for exclusions at each stage are noted where feasible.

### Review 4b: Acceptability of Household and Community-Based TB Screening in High Burden Communities: a Systematic Literature Review

Forty-seven studies met the eligibility criteria for inclusion. See Figure 1 in the review for details on the study selection process.

## Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

## Rating Scheme for the Strength of the Evidence

Grading of Recommendations Assessment, Development and Evaluation (GRADE) Levels of Evidence

Quality of Evidence	Rationale
<b>High</b>	Further research is very unlikely to change confidence in the estimate of effect.
<b>Moderate</b>	Further research is likely to have an important impact on confidence in the effect.
<b>Low</b>	Further research is very likely to have an important impact on the estimate of effect and is likely to change the estimate.
<b>Very Low</b>	Any estimate of effect is very uncertain.

## Methods Used to Analyze the Evidence

Meta-Analysis

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

## Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse and the World Health Organization (WHO): In order to develop the principles and recommendations for systematic screening for active tuberculosis, WHO commissioned four systematic reviews (see the "Availability of Companion Documents" field).

#### Review 1: The Benefits to Communities and Individuals of Screening for Active Tuberculosis Disease: a Systematic Review

##### Data Synthesis and Analysis

Settings, populations (e.g., homeless, refugees, general population) and screening approach differed considerably. Due to the heterogeneity of the studies, a narrative approach was adopted for data synthesis. A formal meta-analysis was conducted where appropriate, which was only for the treatment outcome analysis. The relative risk (RR) of successful treatment by case-finding method was calculated and pooled with the DerSimonian-Laird random-effects method, which treats studies as a sample of all potential studies, and incorporates an additional between-study component to the estimate of variability. The  $I^2$  statistic was calculated as a measure of the proportion of the overall variation that is attributable to between-study heterogeneity.

##### Quality Assessment

The vast majority of the studies included in this review are observational. Furthermore, the Grading of Recommendations Assessment, Development and Evaluation (GRADE) guidelines identify four key limitations that can lead to a risk of bias in observational studies: 1) failure to develop and apply appropriate eligibility criteria, 2) flawed measurement of both exposure and outcome, 3) failure to adequately control confounding, and 4) incomplete follow-up. In the context of this review, such limitations were assessed for each of the questions being evaluated.

See the review for additional information.

#### Review 2: A Systematic Review of the Sensitivity and Specificity of Symptom- and Chest-Radiography Screening for Active Pulmonary Tuberculosis in HIV-Negative Persons and Persons with Unknown HIV Status

##### Data Extraction

Data were extracted by one reviewer and entered in an Excel database through predesigned electronic forms. The second reviewer checked the extract of all included articles. Discrepancies between the database and the publication were corrected.

##### Assessment of Methodological Quality

The methodological quality of included studies was assessed by two reviewers using the modified Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) instrument. The tool comprises four domains: patient selection, index test, reference standard, and flow and timing. Each domain is assessed in terms of risk of bias, and the first three domains are also assessed in terms of concerns regarding applicability.

The methodological quality assessment was done by discussing all items with two researchers.

##### Data Analysis

Diagnostic two-by-two tables were generated, from which sensitivities and specificities for each index test with 95% confidence intervals were calculated and presented in paired forest plots for each study. In addition, a receiver operating characteristic (ROC) plot of sensitivity versus 1-specificity was used to display the data for each test. If studies showed sufficient clinical homogeneity (e.g., same index test, similar definition of tuberculosis, similar screening population) a meta-analysis of pairs of sensitivity and specificity was done by the use of bivariate random-effects methods. The bivariate model was chosen because reviewers deal with binary decisions for which an implicit threshold is assumed. Forest plots and ROC curves were generated in Review Manager 5.1. The bivariate model was developed in SAS 9.1.

See the review for additional information.

#### Review 3: A Systematic Review of the Number Needed to Screen to Detect a Case of Active Tuberculosis in Different Risk Groups

##### Data Abstraction

Study characteristics and results were abstracted from each included paper and entered into a database according to a standardized protocol. Abstracted data included study design, demographic information about the study population, active case-finding strategy, case definition for tuberculosis (TB), and outcome. If multiple populations or risk groups were screened separately but reported in a single publication, each population was abstracted separately.



## Data Analysis

The primary outcome of interest in this review was the number of persons required to be screened in order to detect a single case of active TB (number needed to screen, or NNS). For each individual study, this was computed indirectly as the inverse of the prevalence of TB detected through direct screening. Due to substantial known heterogeneity between studies in terms of population composition, screening and diagnostic approaches, background prevalence of TB, human immunodeficiency virus (HIV), and other risk factors, it was not possible to calculate meaningful aggregate estimates of NNS across all studies. Studies were stratified according to a number of these features in an effort to create more homogenous subgroups for analysis.

See the review for additional information.

### Review 4a: Acceptability of TB Screening among At-Risk and Vulnerable Groups: a Systematic Qualitative/Quantitative Literature Metasynthesis

## Data Items

A data extraction form was developed. Data were extracted into an Excel spread sheet by a single reviewer per group. When acceptability was not measured or described as a formal topic, the refusal rate in screening studies was considered a proxy for lack of acceptability of screening. If the proportion screened was available from the abstract, the datum was extracted into the data set.

See the review for additional information.

### Review 4b: Acceptability of Household and Community-Based TB Screening in High Burden Communities: a Systematic Literature Review

## Data Extraction Process

A data-extraction form containing all relevant information for data extraction was developed in MS Word. One reviewer extracted all relevant data-items from the included studies using this data-extraction form, except those in Spanish and Portuguese which were extracted by the author. A second reviewer checked the extraction of a 25% subsample of the articles and extracted data from Spanish and Portuguese sources. Inconsistencies were discussed to obtain consensus.

See the review for additional information.

## Methods Used to Formulate the Recommendations

### Expert Consensus

## Description of Methods Used to Formulate the Recommendations

A scoping meeting was organized by the World Health Organization (WHO) in June 2011 to assess the need to develop guidelines on tuberculosis (TB) screening, to scope the evidence, identify key research questions and related knowledge gaps, define PICO (Population, Intervention, Comparator, Outcome) questions and develop a plan of work, including establishing a steering group and a Guideline Development Group. After an open call for applications, four systematic reviews were subsequently commissioned on:

- The general benefits of TB screening (Review 1)
- The sensitivity and specificity of different screening tools and algorithms (Review 2)
- The number needed to screen to detect one case of TB in different risk groups (Review 3)
- The acceptability of screening in different risk groups (Review 4)

A meeting to review the data was organized for June 2012, at the time when three systematic reviews had been almost finalized, and one review had just started. At that meeting preliminary findings were discussed, and a plan was developed to complete the final analyses before the final guideline meeting.

The final guideline meeting was convened in October 2012. Ahead of the meeting, the final reports of the systematic reviews, the tables showing the Grading of Recommendations Assessment, Development and Evaluation (GRADE) tables and the decision tables were circulated to members. Each decision table and its related GRADE tables were discussed separately, and the guideline group either developed recommendations or decided that there was insufficient evidence to develop a recommendation.

See Section 4.2 in the original guideline document for information on GRADE tables and decision tables.

Consensus was sought for each recommendation, and all members of the group were asked if they agreed with the final recommendation. When consensus was not reached, different options for the recommendation were drafted and voted on; divergent opinions were recorded. Voting was necessary for only one recommendation.

## Grading the Recommendations

Recommendations on the specific risk groups that should be considered for screening were graded as strong or conditional (see the "Rating Scheme for the Strength of the Recommendations" field). The grading of the recommendations was based on:

- The strength of the direct evidence of benefit compared with the harms of screening in a given risk group
- Indirect evidence of the benefit of screening, including evidence on the burden of undiagnosed TB in a given risk group and evidence of the risk of poor health outcomes in the absence of treatment or caused by delays in diagnosis and treatment
- The feasibility, acceptability and cost implications of screening, including the possibility of efficiently identifying and reaching people in a given risk group without violating basic ethical principles

The overall quality of the direct evidence of benefit compared with evidence of harm ranged from very low to low for all risk groups considered. The values and preferences of the members of the Guideline Development Group therefore significantly influenced the interpretation of indirect evidence and the grading of the recommendations.

The Guideline Development Group placed high value on ensuring that TB is diagnosed early in groups that have a particularly high likelihood of undetected TB and a high risk of poor health outcomes in the absence of early diagnosis and treatment, even if direct evidence of benefit from screening was lacking. Therefore, strong recommendations have been made despite the lack of high-quality direct evidence for three risk groups.

However, the Guideline Development Group also strongly emphasized the need for careful prioritization that considers the opportunity costs of screening, both across risk groups and in relation to other interventions aimed at improving early diagnosis, treatment and prevention. Therefore, owing to the lack of high-quality direct evidence comparing benefits with harms and on the cost effectiveness of screening, the majority of the recommendations made about screening specific risk groups are conditional. Furthermore, the Guideline Development Group emphasized the importance of avoiding the risk of doing harm through screening – that is, both harm to the screened individual and indirect harm by misusing health resources. While the Guideline Development Group did not make any specific negative recommendations (that is, recommendations not to screen in certain situations), the group agreed that a key principle is to avoid indiscriminate screening, and that risk groups should be carefully prioritized for screening using set criteria (outlined in Section 7.2 in the original guideline document).

Graded recommendations have not been made on which algorithms should be used for screening and diagnosing TB in specific risk groups. Instead, options for screening and diagnosis have been developed; these are presented with remarks about the key issues that should be considered when choosing algorithms for different risk groups, and different epidemiological situations and health systems (see section 8 in the original guideline document for remarks to recommendations).

## Rating Scheme for the Strength of the Recommendations

### Strength of Recommendations

A strong recommendation is one for which the desirable effects of adhering to the recommendation are judged to clearly outweigh the undesirable effects; for these recommendations screening is judged to be feasible, acceptable and affordable in all settings. The Guideline Development Group placed a high value on ensuring that tuberculosis (TB) is diagnosed early in groups with a particularly high likelihood of having undetected TB and at a high risk for poor health outcomes in the absence of early diagnosis and treatment even if direct evidence of the benefits of screening were lacking. This is the rationale for making strong recommendations despite a lack of high-quality direct evidence for some risk groups.

A conditional recommendation is one for which the desirable effects of adhering to the recommendation probably outweigh the undesirable effects but the trade-offs, cost effectiveness, feasibility or affordability, or a combination of these, are uncertain. Reasons for uncertainty may include:

- A lack of high-quality evidence to support the recommendation
- Evidence of limited benefits from implementing the recommendation
- High costs, or low feasibility or acceptability, or a combination of these

The degree of uncertainty about the trade-offs between the desirable effects and undesirable effects of adhering to each of the conditional recommendations varies across settings, and depends on the epidemiological situation and the health system. Therefore, a conditional recommendation in this guideline implies that:

- The appropriateness of adhering to the recommendation needs to be assessed in each setting
- There is a need to prioritize screening across risk groups in each setting

## Cost Analysis

Cost effectiveness can be estimated in relation to the number of additional true tuberculosis (TB) cases detected, the reduction in morbidity, the reduced time that a person remains infectious, and the reductions in transmission, incidence and mortality. Cost benefit can be estimated in terms of future costs saved for the individual, the health sector or society, or all of these. The total cost depends on the number needed to screen, the algorithm used for screening and diagnosis, the method used to reach people for screening, and the direct and indirect costs incurred for the screened individuals.

## Method of Guideline Validation

External Peer Review

Internal Peer Review

## Description of Method of Guideline Validation

Draft guidelines were circulated to a group of peer reviewers, consisting of all staff of the Stop Tuberculosis (TB) Department at World Health Organization's (WHO's) headquarters and staff of other selected departments, regional TB advisers, managers of selected national TB programmes, other national stakeholders involved in TB care and control in selected countries, working groups in the Stop TB Partnership, organizations providing technical support to TB care and control activities, and individuals with expertise in TB care and control (see Annex IV in the original guideline document).

## Evidence Supporting the Recommendations

### Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

## Benefits/Harms of Implementing the Guideline Recommendations

### Potential Benefits

- Screening for active tuberculosis (TB) ensures that active TB is detected early and treatment is initiated promptly, with the ultimate aim of reducing the risk of poor treatment outcomes, health sequelae and the adverse social and economic consequences of TB, as well as helping to reduce TB transmission.
- When prioritizing which groups to screen, the following factors should be considered for each risk group.
  - Potential benefits for the individual: These benefits include the health, social and economic benefits of early diagnosis and treatment of TB. In principle, the potential benefits are greater for persons who have a high risk of delaying diagnosis because there are barriers to health care, or they have a high risk of poor treatment outcome when diagnosis is delayed—for example, because their immune system is compromised.
  - Potential impact on transmission within and beyond the risk group: The potential of screening to have an impact on transmission is theoretically highest in congregate settings where there is a high rate of transmission and where there is also substantial in-migration and out-migration. In principle, the larger the risk group that is screened, the larger the potential impact on transmission in the community. However, when the TB burden is highly concentrated in a few high-risk groups, the largest impact on overall transmission may come from screening highly selected groups, and these may be small in size.

See also Review 1 (see the "Availability of Companion Documents" field) for more information about the benefits of screening.

## Potential Harms

### Potential Risks for the Individual

These risks are associated with the process of screening and diagnosis and include the time, inconvenience and cost of screening, as well as the result of screening. Harms from the results of screening include the unintended negative effects of being correctly diagnosed (which may cause stigma or discrimination) and harm caused by a false-positive diagnosis or a false-negative diagnosis. Harms from screening include the unintended negative effects of being correctly diagnosed (which may cause stigma or discrimination) and harm caused by a false-positive or a false-negative diagnosis, as well as inappropriate use of health-care resources.

## Qualifying Statements

### Qualifying Statements

- The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the World Health Organization (WHO) concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.
- The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by the WHO in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.
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## Implementation of the Guideline

### Description of Implementation Strategy

All of the partners included in the guideline-development process have a wide network of experts in different areas and countries who provide technical assistance to national tuberculosis (TB) control programmes and other country partners engaged in TB care and control; these experts can help with local adaptation of the recommendations and algorithm options. The guideline will be widely disseminated, as will technical assistance from World Health Organization (WHO) and its partners, to help adapt the guideline to local situations and to mobilize resources.

The impact of the guideline should be evaluated by collecting data from the routine operation of TB surveillance systems (that is, by monitoring case detection, and using disaggregated data on the source of detection and type of case-finding strategy) and through operational research.

Practical tools for assessing the TB situation, prioritizing risk groups and creating national screening strategies for TB were to have been developed during 2013–2014.

### Implementation Tools

#### Audit Criteria/Indicators

#### Clinical Algorithm

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

# Categories

## IOM Care Need

Getting Better

Living with Illness

Staying Healthy

## IOM Domain

Effectiveness

Patient-centeredness

# Identifying Information and Availability

## Bibliographic Source(s)

World Health Organization (WHO). Systematic screening for active tuberculosis: principles and recommendations. Geneva (Switzerland): World Health Organization (WHO); 2013. 133 p. [103 references]

## Adaptation

Not applicable: The guideline was not adapted from another source.

## Date Released

2013

## Guideline Developer(s)

World Health Organization - International Agency

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See the original guideline document for members of the WHO Secretariat and the peer reviewers.

## Financial Disclosures/Conflicts of Interest

Conflict-of-interest forms were collected from all members before each meeting, and from peer reviewers who provided comments. None of the experts declared any conflicts of interest that were judged to significantly affect the development of the guideline.

## Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

## Guideline Availability

Electronic copies: Available from the [World Health Organization \(WHO\) Web site](#) .

Print copies: Available from the WHO Press, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland; Phone: +41 22 791 3264; Fax: +41 22 791 4857; E-mail: [bookorders@who.int](mailto:bookorders@who.int).

## Availability of Companion Documents

The following are available:

- Review 1: Kranzer K, Afnan-Holmes H, Tomlin K, Golub JE, Shapiro A, Schaap A, Corbett EL, Lönnroth K, Glynn JR. The benefits to communities and individuals of screening for active tuberculosis disease: a systematic review. *Int. J. Tuberc. Lung Dis.* 2013 Apr; 17(4): 432-46. Electronic copies: Available from the [World Health Organization \(WHO\) Web site](#) .
- Review 2: van't Hoog AH, Langendam MW, Mitchell E, Cobelens FG, Sinclair D, Leeftang MMG, Lönnroth K. A systematic review of the sensitivity and specificity of symptom- and chest-radiography screening for active pulmonary tuberculosis in HIV-negative persons and persons with unknown HIV status. Geneva (Switzerland): World Health Organization (WHO); 2013 Mar. 66 p. Electronic copies: Available from the [WHO Web site](#) .
- Review 3: Shapiro AE, Chakravorty R, Akande T, Lönnroth K, Golub JE. A systematic review of the number needed to screen to detect a case of active tuberculosis in different risk groups. Geneva (Switzerland): World Health Organization (WHO); 2013 Jan. 86 p. Electronic copies: Available from the [WHO Web site](#) .
- Review 4a: Mitchell EMH, Shapiro A, Golub J, Kranzer K, Portocarrero AV, Antillón Najlis C, Ngamvithayapong-Yanai J, Lönnroth K. Acceptability of TB screening among at-risk and vulnerable groups: a systematic qualitative/quantitative literature metasynthesis. Geneva (Switzerland): World Health Organization (WHO); 67 p. Electronic copies: Available from the [WHO Web site](#) .
- Review 4b: Mitchell EMH, den Boon S, Lönnroth K. Acceptability of household and community-based TB screening in high burden

communities: a systematic literature review. Geneva (Switzerland): World Health Organization (WHO); 47 p. Electronic copies: Available from the [WHO Web site](#) .

- Improving early detection of active TB through systematic screening. Factsheet. Geneva (Switzerland): World Health Organization (WHO); 2013. 2 p. Electronic copies: Available from the [WHO Web site](#) .
- Modelled yield of different screening and diagnostic algorithms. Geneva (Switzerland): World Health Organization (WHO); 7 p. Electronic copies: Available from the [WHO Web site](#) .
- GRADE tables. Geneva (Switzerland): World Health Organization (WHO); 10 p. Electronic copies: Available from the [WHO Web site](#) .
- Decision tables. Geneva (Switzerland): World Health Organization (WHO); 54 p. Electronic copies: Available from the [WHO Web site](#) .
- Scoping meeting for the development of guidelines on screening for active TB. Geneva (Switzerland): World Health Organization (WHO); 2011 Jun. 24 p. Electronic copies: Available from the [WHO Web site](#) .
- WHO handbook for guideline development. Geneva (Switzerland): World Health Organization; 2014. 167 p. Electronic copies: Available from the [WHO Web site](#) .

In addition, proposed indicators for monitoring and evaluation are available in section 10 in the [original guideline document](#)

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## Patient Resources

None available

## NGC Status

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